

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Brian Trinque on January 29, 2010.

Claims 1, 6, 8, 12, and 13 are cancelled.

Claims 17-19, 23, and 24 are amended as follows:

17. (Currently Amended) A method of treating a proliferative disorder, wherein the proliferative disorder is selected from lung cancer, prostate cancer, bladder cancer, head and neck cancer, colon cancer, sarcoma and lymphoma, said method comprising sequentially administering to a subject, ~~simultaneously, sequentially or separately,~~ 1-(2-C-cyano-2-deoxy- β -D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or metabolite thereof, wherein the metabolite is 1-(2-C-Cyano-2-deoxy- β -D-arabino-pentafuranosyl)-cytosine, and roscovitine.

18. (Currently Amended) A method according to claim 17 which comprises administering roscovitine, to a subject prior to sequentially ~~or separately~~ administering

Art Unit: 1623

1-(2- C-cyano-2- ~~deoxy~~deoxy- β -D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or metabolite thereof, to said subject.

19. (Currently Amended) A method according to claim 17 which comprises administering 1- (2- C-cyano-2- ~~deoxy~~deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine, or metabolite thereof, to a subject prior to sequentially ~~or separately~~ administering roscovitine to said subject.

23. (Currently Amended) A method according to claim 17 wherein the roscovitine and 1- (2- C-cyano-2- ~~deoxy~~deoxy- β -D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or metabolite thereof, are each administered in a therapeutically effective amount with respect to the individual components.

24. (Currently Amended) A method according to claims 17 wherein the roscovitine and 1-(2- C-cyano-2- ~~deoxy~~deoxy- β -D-arabino-pentofuranosyl)-N4-palmitoyl cytosine, or metabolite thereof, are each administered in a subtherapeutic amount with respect to the individual components.

Detailed Action

This office action is a response to applicant's communication submitted November 6, 2009 wherein claims 1, 8, 13, 17-19, 23, and 24 are amended and claims 2-5, 7, 9-11, 14-16, 20-22, and 25-31 are cancelled. This application is a national stage application of PCT/GB04/05081, filed December 3, 2004, which claims priority to foreign application GB0328180.5, filed December 3, 2004.

Claims 17-19, 23, and 24 are pending in this application.

Claims 17-19, 23, and 24 as amended are examined on the merits herein.

Reasons for Allowance

The declaration of Simon R. Green under 37 CFR 1.132, submitted November 6, 2009, has been fully considered and entered into the record. The declaration is discussed further below as it relates to the rejections of record in the previous office action.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 7 and 28-31 under 35 USC 101, for reciting a use without setting forth any method steps, has been fully considered and found to be persuasive to remove the rejection as the rejected claims have been cancelled. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 7 and 28-31 under 35 USC 112, first paragraph, for reciting a use without setting forth any method steps, has been fully considered and found to be persuasive to remove the rejection as the rejected claims have been cancelled. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 1-4, 6-15, 17-26, and 28-31 under 35 USC 112, second paragraph, for indefinitely reciting metabolites of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to specify that a metabolite of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine refers to the specific compound 1-(2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)- cytosine. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 1, 2, 5-9, 12-20, 23-26, and 29-31 under 35 USC 112, first paragraph, for lacking enablement for all possible CDK inhibitors, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to limit the scope to only one singe CDK inhibitor, roscovitine. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 1-4, 6-15, 17-26, and 28-31 under 35 USC 112, first paragraph, for lacking enablement for all possible metabolites of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to limit the scope to only one singe metabolite. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of instant claims 1-31 under 35 USC 112, first paragraph, for lacking enablement for methods of treating all possible cancers and proliferative disorders, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to limit the scope to certain specific cancers that are enabled by Applicant's disclosure. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of claims 1-4, 6-15, 17-26, and 28-31 under 35 USC 103(a) for being obvious over Kameko et al. in view of Altieri et al., has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to limit their scope to a single embodiment for which unexpected results have been demonstrated. Therefore the rejection is withdrawn.

Applicant's amendment, submitted November 6, 2009, with respect to the rejection of claims 1-31 under 35 USC 103(a) for being obvious over Hanaoka et al. in view of Altieri et al., has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to limit their scope to a single embodiment for which unexpected results have been demonstrated. Therefore the rejection is withdrawn.

Currently claims 17-19, 23, and 24 are pending in this application and have been examined on the merits herein. Applicant's amendment submitted November 6, 2009, and the enclosed examiner's amendment, are seen to be persuasive to remove all rejections of record in the previous office action and place the application in condition for allowance. Reasons for allowance are as follows:

The claims are seen to be adequately described and enabled by the specification as originally filed. Although the previously filed claims were indefinite and lacked utility and enablement as described in the previous office action of May 7, 2009. the scope of the claims has been narrowed by the most recent amendment to describe the specific combination of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine or 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)- cytosine with roscovitine. This combination is clearly enabled by the specification as originally filed, which clearly shows how to make and use these compounds for treating these specific cancers. Therefore the claims meet the requirements of 35 USC 112.

Furthermore the claimed invention is novel and non-obvious over the prior art. The combination of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine and roscovitine is not disclosed anywhere in the prior art. Although as described in the previous office action, the two components are known individually to be useful for treating various cancers, Applicant has demonstrated unexpected results for the sequential combination of these compounds when used to kill cancer cells. Specifically the declaration of Simon R. Green submitted November 6, 2009, discloses that sequential administration of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-cytosine (CNDAC) and roscovitine (Sel) produces a superadditive increase in the percent of apoptotic cells in two tumor cell lines. Because 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-N4-palmitoyl cytosine is a prodrug of 1- (2- C-cyano-2-deoxy- β -D-arabino -pentofuranosyl)-cytosine, as described in p. 4 lines 9-21 of the specification, it would be expected to produce the same effects in combination with roscovitine as the metabolite. This superadditive effect is unexpected and therefore serves to overcome the *prima facie* case of obviousness made in the previous office action. Therefore the claims meet the requirements of 35 USC 102 and 103.

Accordingly, Applicant's amendment and declaration submitted November 6, 2009, and the enclosed examiner's amendment, are sufficient to remove all rejections made in the prior office action as discussed above and to place the application in condition for allowance.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled, "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/581,585
Art Unit: 1623

Page 10

/Eric S Olson/
Examiner, Art Unit 1623
1/29/2010